REMARKS

Applicants' Representative thanks Examiner C. Chang for the helpful and courteous discussion of June 4, 2002.

Upon entry of this amendment, claims 90-111 will be pending. Claims 90, 96, 99, and 105 have been amended. Claims 108-111 have been added. No new matter has been added.

As per 37 C.F.R. § 1.121(c)(1), amendments are presented in clean form in the body of this filing and in marked-up form in the attached Appendix.

I. The Rejection Of Claims 90-107 For Non-Statutory Double Patenting

Claims 90-107 stand provisionally rejected for non-statutory double patenting over claims 1-177 of U.S. Patent Application No. 09/159,105 ("the '105 application") in view of MedLine 98242495 ("Feghali").

The Office has maintained this rejection "for the reasons of record" (Office Action, page 2, paragraph #2). The non-final Office Action dated 19-Sep-01 ("the non-final Action") asserted that claims 1-177 of the '105 application recite treating a disorder generically embraced by the present claims and that the disclosed compounds encompass those recited in the present claims (September 19 Office Action, page 2, lines 6-10).

Applicants respectfully traverse.

According to the M.P.E.P., a provisional double patenting rejection may be due between "two copending applications filed by the same inventive entity, or by different

inventive entities having a common inventor, and/or by a common assignee." M.P.E.P. § 804.I.B., page 800-19 (8th Ed., August 2001).

The present application is assigned to "GPI NIL Holdings, Inc." which is now entirely owned by Guilford Pharmaceuticals Inc. The '105 application is not assigned to GPI NIL Holdings, Inc. or any company related to Guilford Pharmaceuticals Inc. Applicants have therefore been unable to obtain a copy of the '105 application. However, WO 99/14,998 (of record in this case in Form PTO-892 of Paper No. 17) claims priority to and therefore likely corresponds to the '105 application. WO 99/14,998 has no common inventors with the '105 application. The '105 application is therefore not an application "filed by the same inventive entity, or by different inventive entities having a common inventor, and/or by a common assignee" and cannot support a provisional double patenting rejection. The rejection should thus be withdrawn.

II. The Rejections Of Claims 90-107 Under 35 U.S.C. § 103(a)

Claim 90-107 stand rejected under 35 U.S.C. § 103(a) on two grounds.

1. The Rejection Over The '256, '449, and '957 Patents, the '105 Application, And Feghali

Claim 90-107 stand rejected under 35 U.S.C. § 103(a) over U.S. Patent No. 5,721,256 ("the '256 patent"), No. 5,874,449 ("the '449 patent"), or No. 5,968,957 ("the '957 patent") in view of U.S. Patent Application No. 09/159,105 and MEDLINE 98242495 ("Feghali").

This ground of rejection would be obviated by the proposed amendment.

The Office has maintained this rejection "for the reasons of record" (Office Action, page 2, paragraph #3). The non-final Action asserted that the '256, '449, and '947 patents disclose treating a neurological disorder with compounds that are "alternative choices for the instantly claimed compounds" (non-final Action, page 2, last 10 lines).

The '256 patent discloses pyrrolidine compounds with a ketone, carboxylic ester, or amide group alpha to the ring nitrogen. The '449 patent discloses pyrrolidine compounds with a thioester group alpha to the ring nitrogen. The '957 patent discloses pyrrolidine compounds with a carboxylic ester group alpha to the ring nitrogen.

The present claims as amended have substituents alpha to the ring nitrogen that have neither structural similarity nor bioisosteric relationship with those in the '256, '449, and '947 patents. Consequently, this rejection does not apply to the present claims as amended.

2. The Rejection Over The '256 Patent, King, And Patani

Claim 90-107 stand rejected under 35 U.S.C. § 103(a) over the '256 patent in view of F.D. King, Med. Chem.: Principle & Practice (1994) 206 ("King") or G.P. Patani et al., Chem. Rev., 1996, Vol. 96, p. 3147 ("Patani").

This ground of rejection would be obviated by the proposed amendment.

The rejection is based on the '256 patent's disclosure of pyrrolidine compounds with a "carboxylate" group alpha to the ring nitrogen (Office Action, page 4, paragraph #4). The '256 patent discloses carboxylate esters with neurotrophic activity, but does not disclose carboxylic acids with neurotrophic activity. The claims as amended recite functional groups alpha to the ring nitrogen that are not structurally similar and do not bear a bioisosteric

relationship to the disclosed carboxylate esters, and thus would not have been obvious to a person of skill in the art. Consequently, this rejection does not apply to the present claims as amended.

III. The Rejection Of Claims 90-107 Under 35 U.S.C. § 112

Claim 90-107 stand rejected under 35 U.S.C. § 112 as allegedly indefinite due to the terms "carboxylic acid" and "carboxylic acid isosteres."

This ground of rejection would be obviated by the proposed amendment.

IV. CONCLUSION

Applicants submit that the proposed amendments would place the pending claims in condition for allowance, would raise no new issues, and would not require further search. Applicants request that the Office exercise its discretion under Rule 116 to enter the amendments and allow the resulting claims. If the Office has questions, the Office is invited to call Applicants' Representative directly at (202) 974-6018.

Please charge or credit Deposit Account No. 12-2475 for all fees as needed.

Respectfully submitted,

LYON & LYON LLP

Dated: 1-Jul-2002

By: _____
Rouget F. Henschel
Reg. No. 39,221

633 West Fifth Street, Suite 4700
Los Angeles, California 90071-2066
202-974-6018

APPENDIX A:

MARKED-UP VERSION OF AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph on page 1, lines 6-10, with the following:

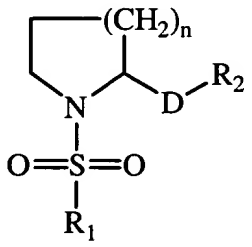
This application is a non-provisional of [continuation-in-part of] U.S. provisional [patent] application serial number 60/087,842 [to Hamilton et al., entitled "N-Linked Sulfonamides of N-Heterocyclic Carboxylic Acids and Carboxylic Acid Isosteres,"] filed June 3, 1998.

APPENDIX B:

MARKED-UP VERSION OF AMENDED CLAIMS

90. (Amended) A method of treating a neurological disorder in an animal, comprising:

administering to the animal an effective amount of a compound to stimulate growth of damaged peripheral nerves or to promote neuronal regeneration, wherein the compound has the formula (I):



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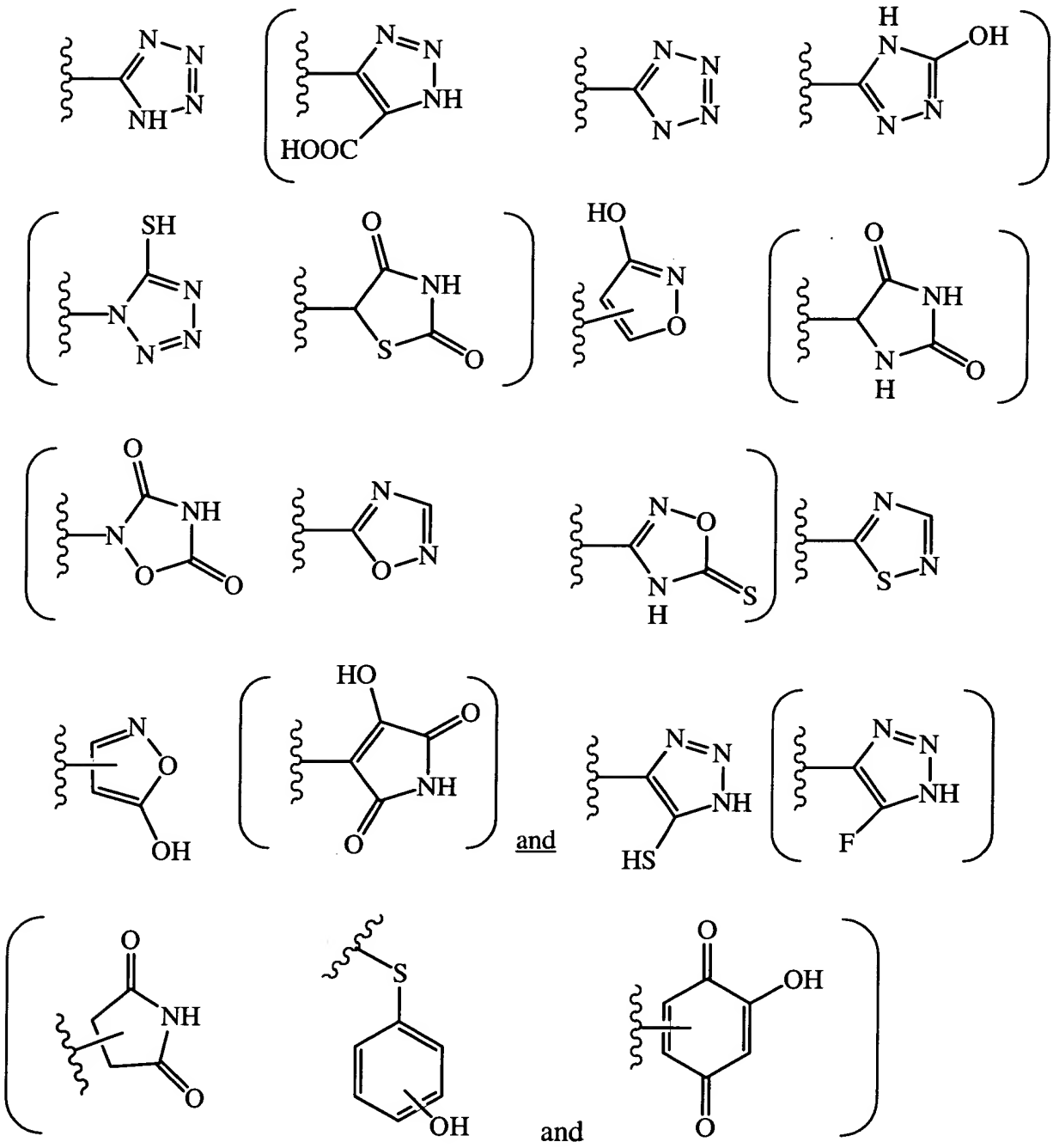
where

n is 1;

R_1 is selected from the group consisting of hydrogen, C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, and heterocycle;

D is selected from the group consisting of a bond, C_1-C_{10} straight or branched chain alkylene, C_2-C_{10} alkenylene, and C_2-C_{10} alkynylene;

R_2 is a carboxylic acid isostere selected from the group consisting of:



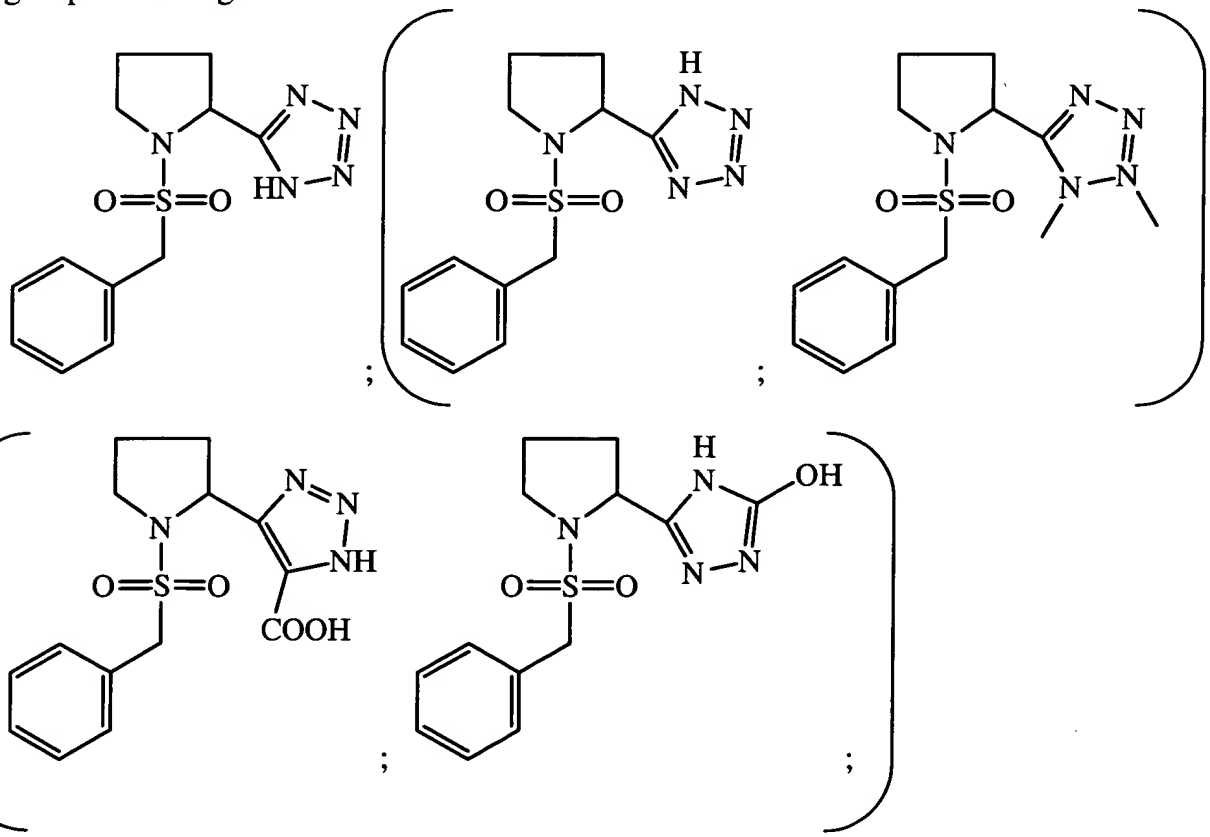
and

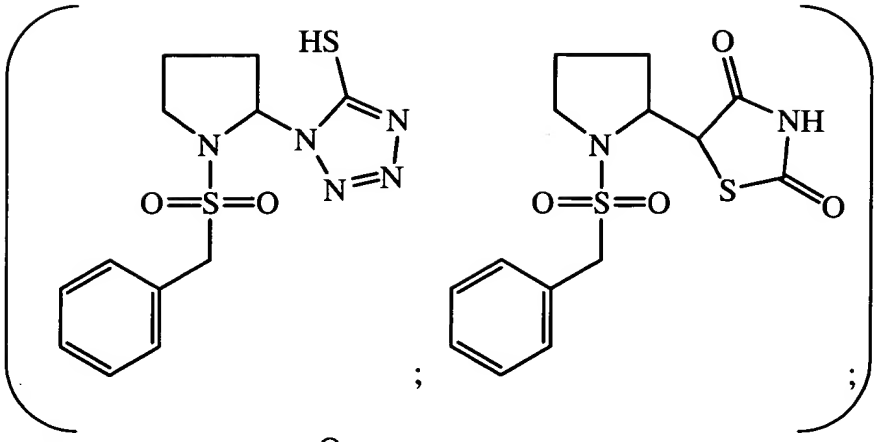
wherein said alkyl, alkenyl, alkylene, alkenylene, alkynylene, aryl, heteroaryl, carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected from R_3, where

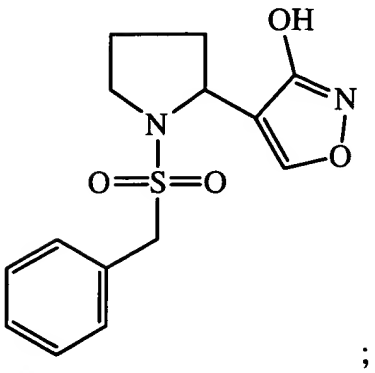
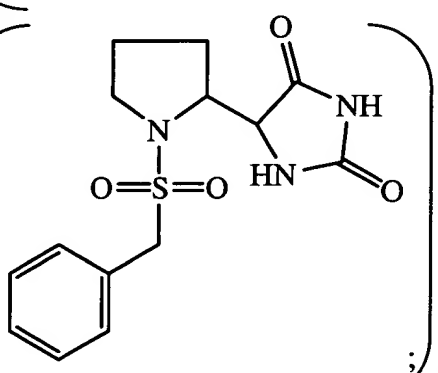
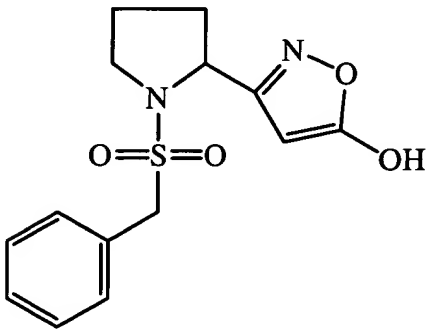
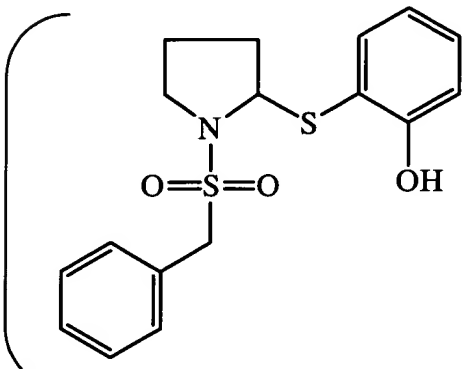
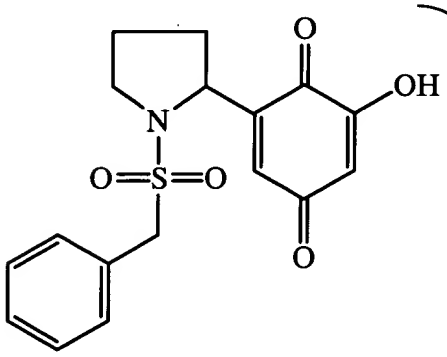
R_3 is selected from the group consisting of hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sufhydryl, thioalkyl, alkylthio, sulfonyl, C_1-C_6 straight or branched chain alkyl, C_2-C_6 straight or branched chain alkenyl or alkynyl, aryl, heteroaryl, carbocycle, heterocycle, and CO_2R_4 where R_4 is selected from the group consisting of hydrogen, C_1-C_9 straight or branched chain alkyl, and C_2-C_9 straight or branched chain alkenyl;

or a pharmaceutically acceptable salt or solvate thereof.

96. (Amended) The method of claim 90, wherein the compound is selected from the group consisting of:

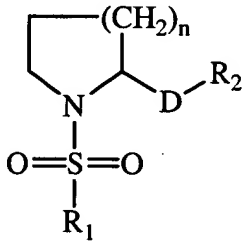




99. (Amended) A method of treating a neurological disorder in an animal, comprising:

administering to the animal an effective amount of a compound to stimulate growth of damaged peripheral nerves or to promote neuronal regeneration, wherein the compound has the formula (I):



I

where

n is 1;

R_1 is selected from the group consisting of hydrogen, C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, and heterocycle;

D is selected from the group consisting of a bond, C_1-C_{10} straight or branched chain alkylene, C_2-C_{10} alkenylene, and C_2-C_{10} alkynylene;

R_2 is a carboxylic acid or carboxylic acid isostere selected from the group consisting of: -COOH, $-SO_3H$, $-SO_2HNR_3$, $-PO_2H$, [$-PO_3(R_3)_2$,] -CN, [$-PO_3(R_3)_2$,] $-PO(OH)(OR_3)$, [$-OR_3$, $-SR_3$, $-NHCOR_3$, $-N(R_3)_2$, $-CON(R_3)_2$, $-CONH(O)R_3$,] –C(O)NHOH, [$-CONHNHSO_2R_3$, $-COHNSO_2R_3$, and $-CONR_3CN$] $-C(O)NHSO_2R_3$, and –CONHCN; wherein said alkyl, alkenyl, alkylene, alkenylene, alkynylene, aryl, heteroaryl, carbocycle, heterocycle, or

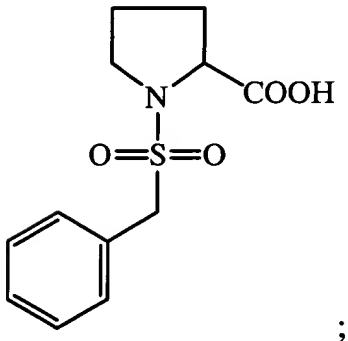
carboxylic acid isostere is optionally substituted with one or more substituents selected from R_3, where

R_3 is selected from the group consisting of hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alkenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C_1-C_6 straight or branched chain alkyl, C_2-C_6 straight or branched chain alkenyl or alkynyl, aryl, heteroaryl, carbocycle, heterocycle, and CO_2R_4 where R_4 is selected from the group consisting of hydrogen, C_1-C_9 straight or branched chain alkyl, and C_2-C_9 straight or branched chain alkenyl;

or a pharmaceutically acceptable salt or solvate thereof.

105. (Amended) The method of claim 99, wherein the compound is selected from the group consisting of:

[(2S)-1-(phenylmethyl)sulfonyl-2-hydroxymethyl pyrrolidine;]



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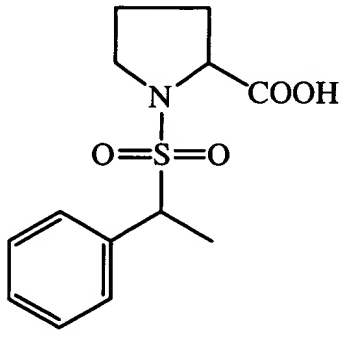

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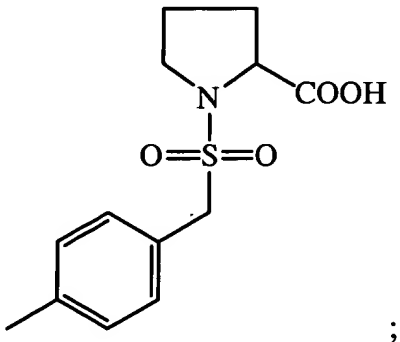

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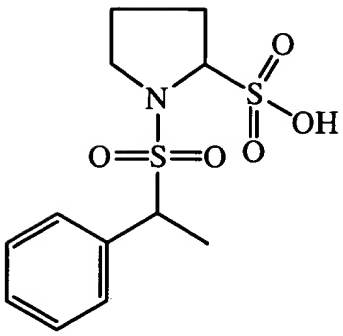
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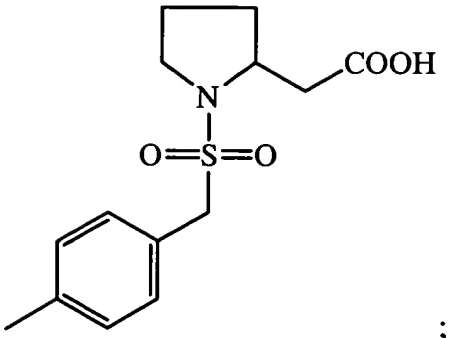
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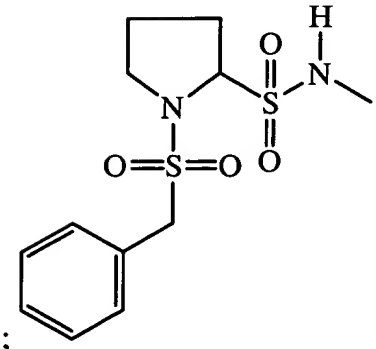
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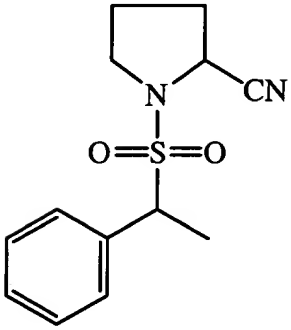
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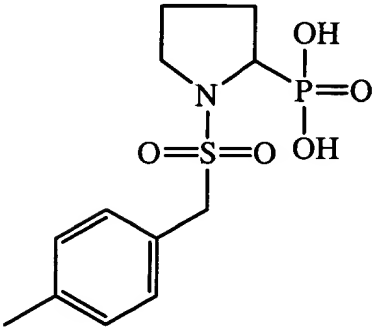
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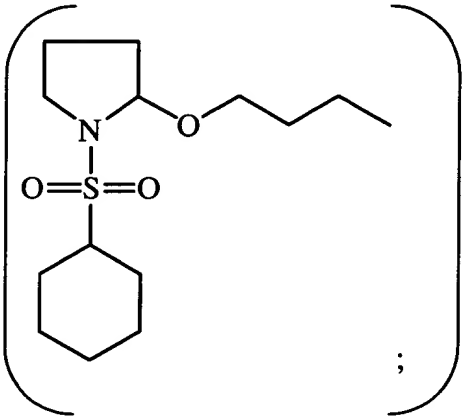
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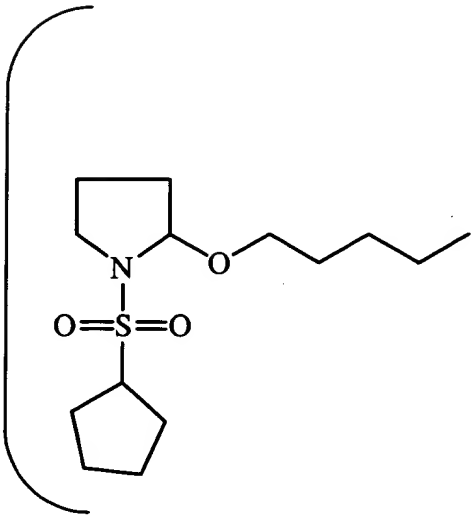
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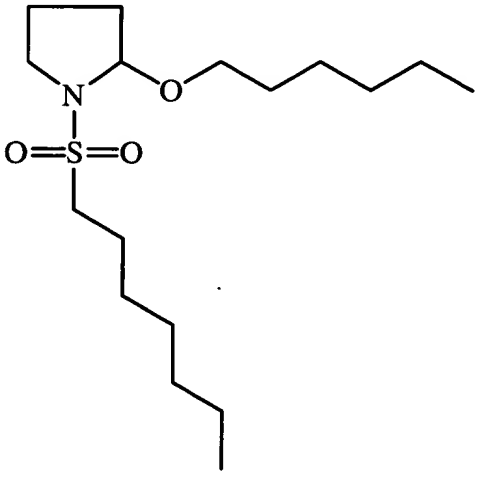
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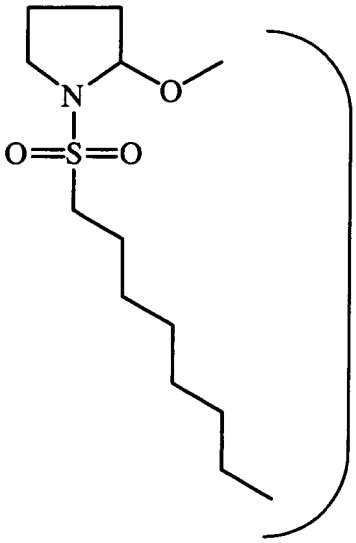

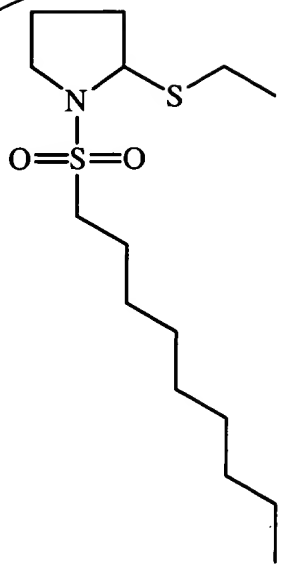
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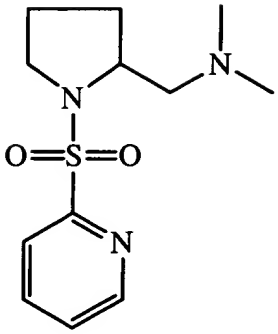
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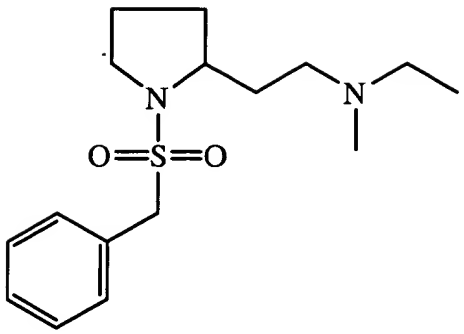
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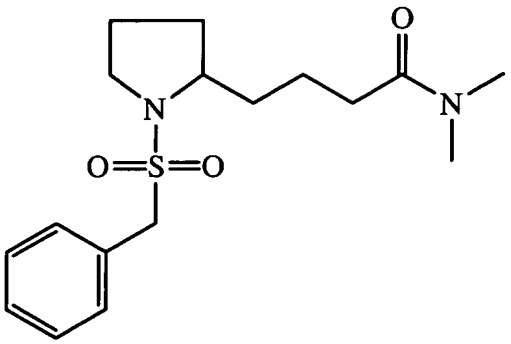
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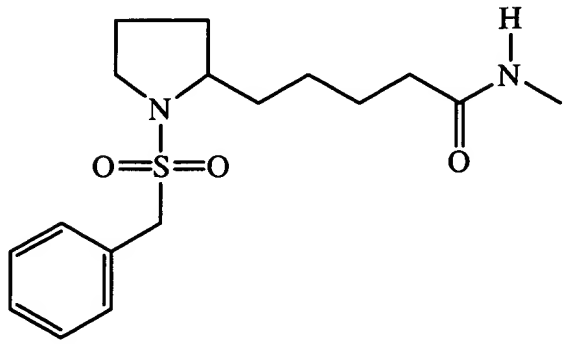
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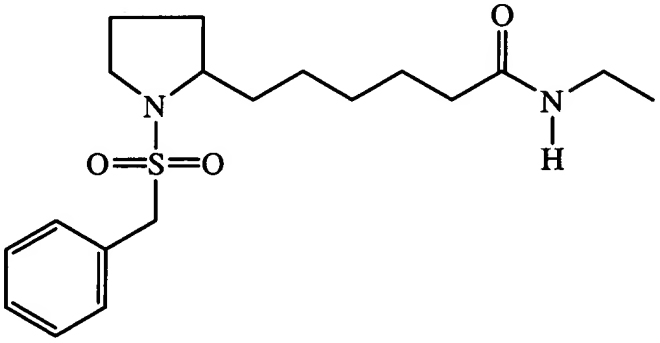
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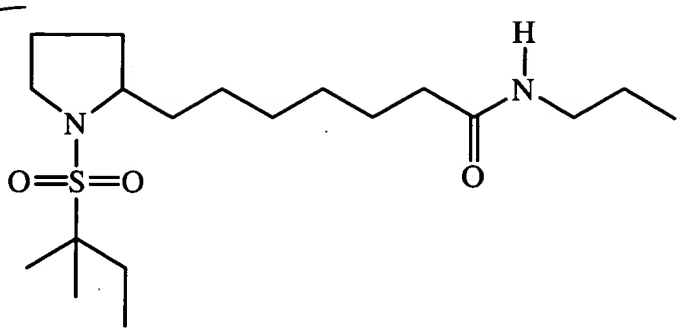
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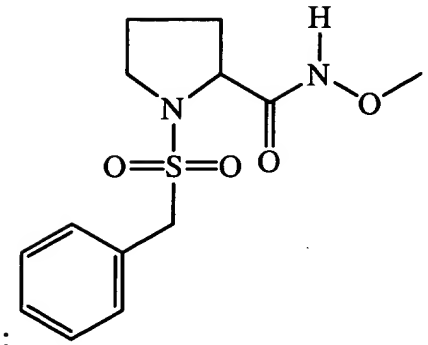
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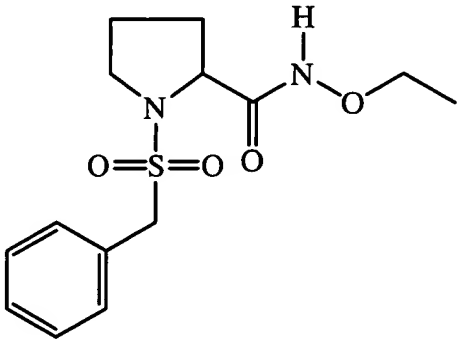
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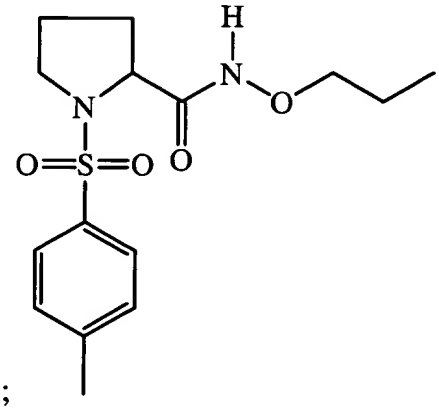
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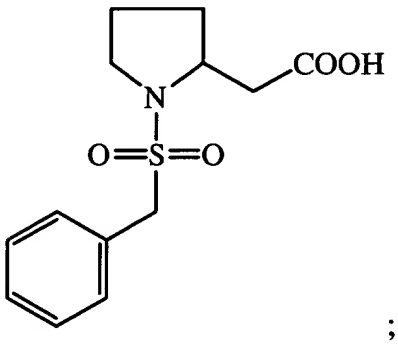
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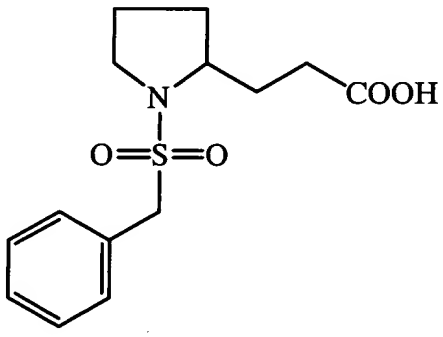
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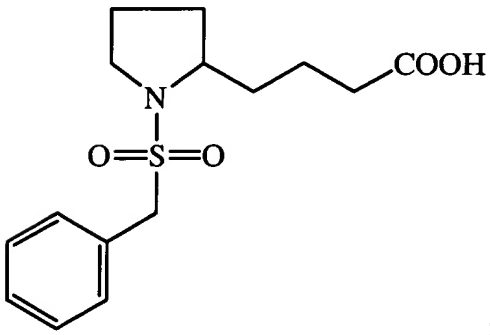
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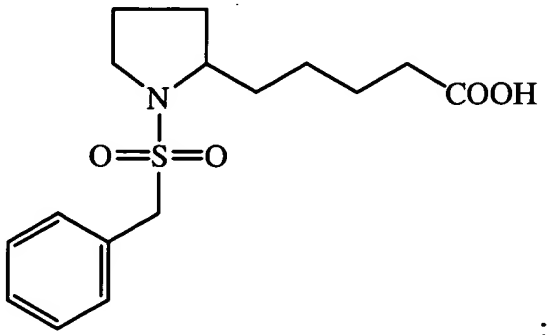
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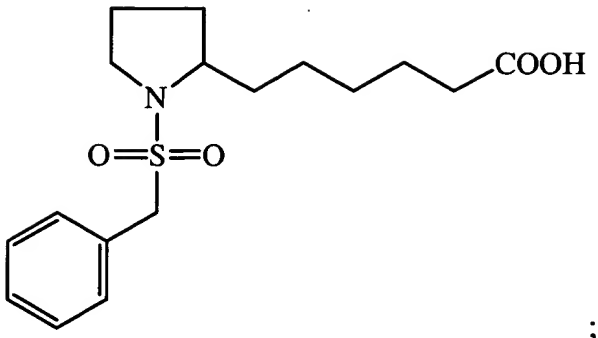
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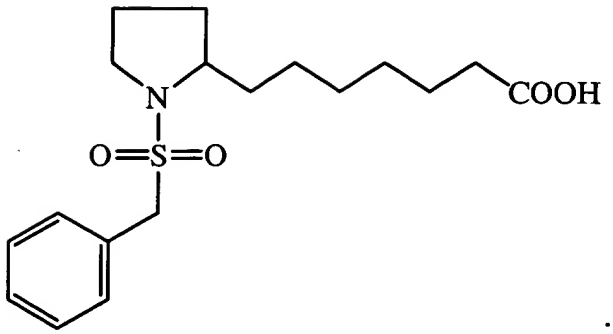
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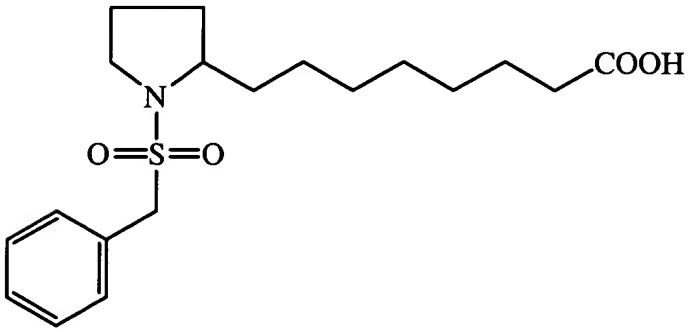
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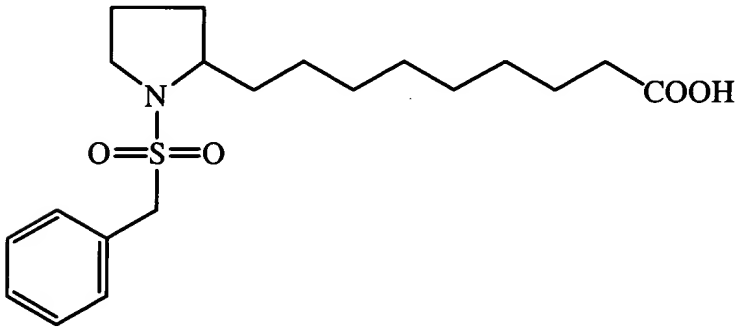
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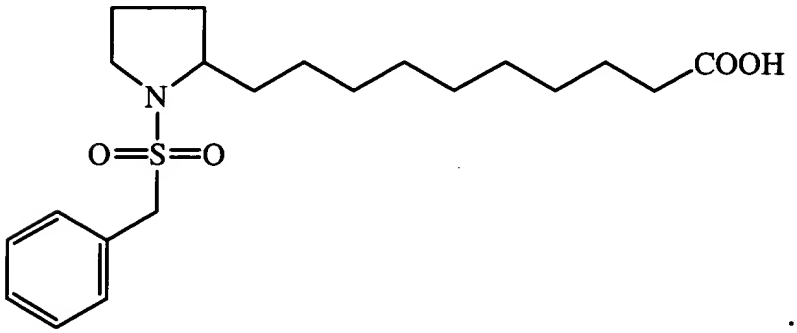
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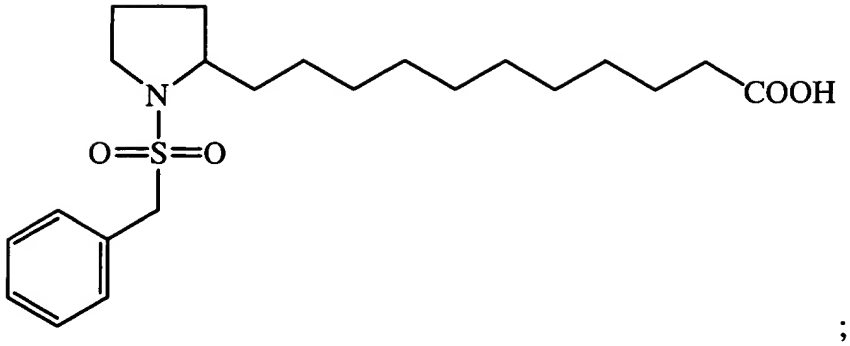

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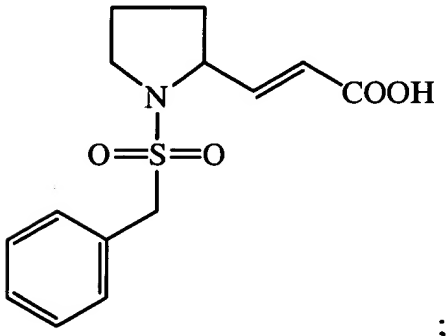

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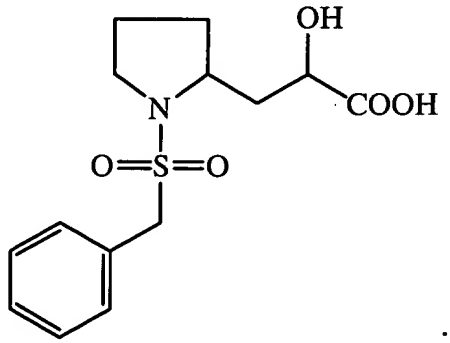

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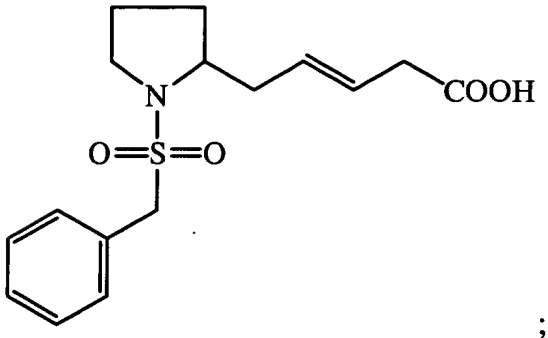

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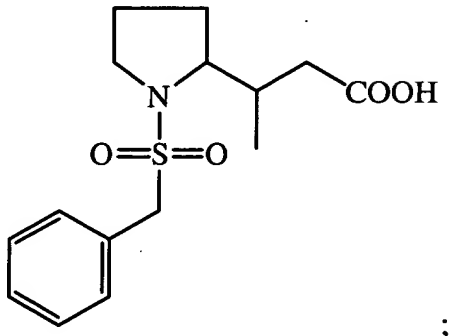

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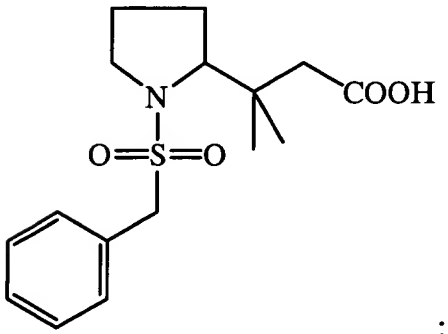

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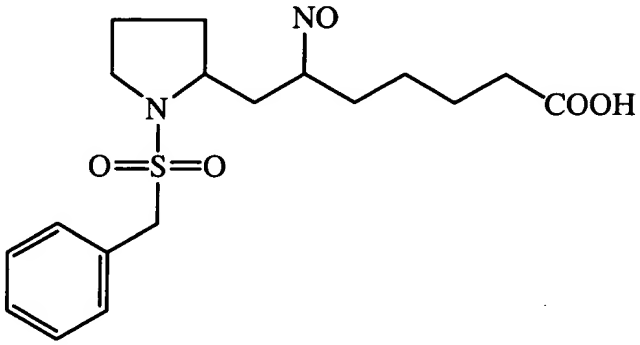

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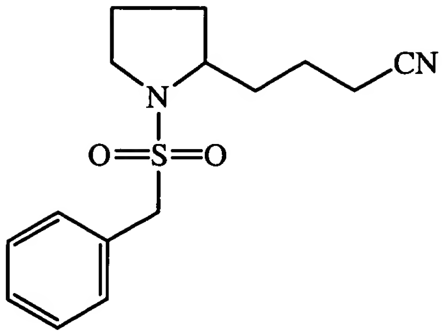

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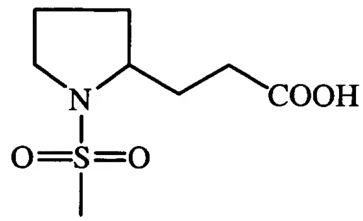

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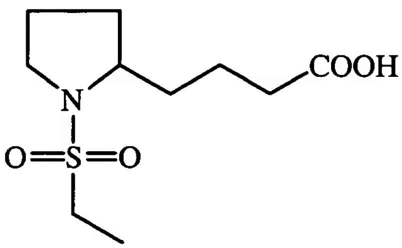

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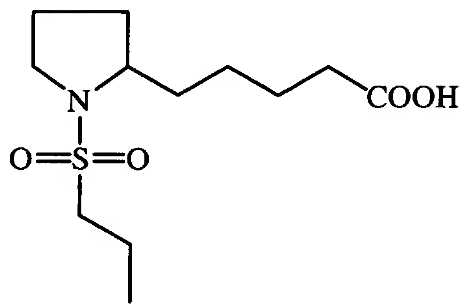

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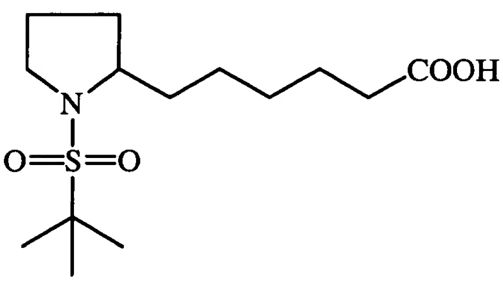

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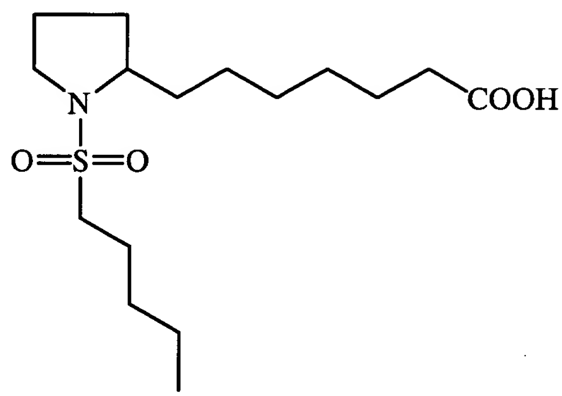

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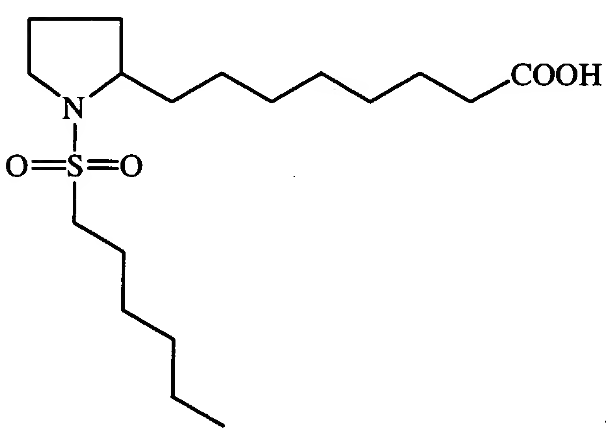

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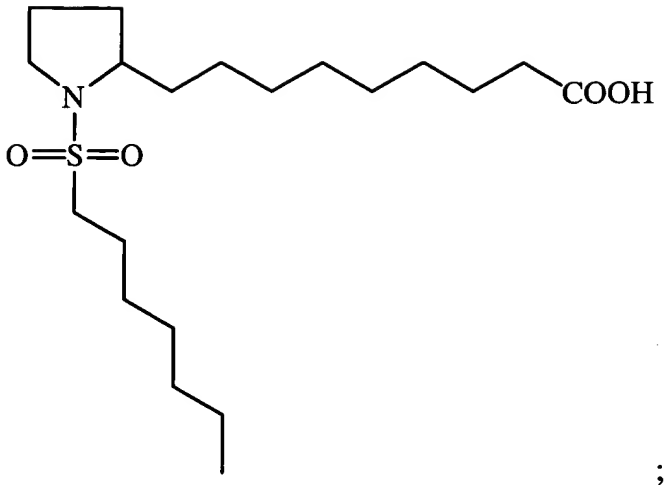
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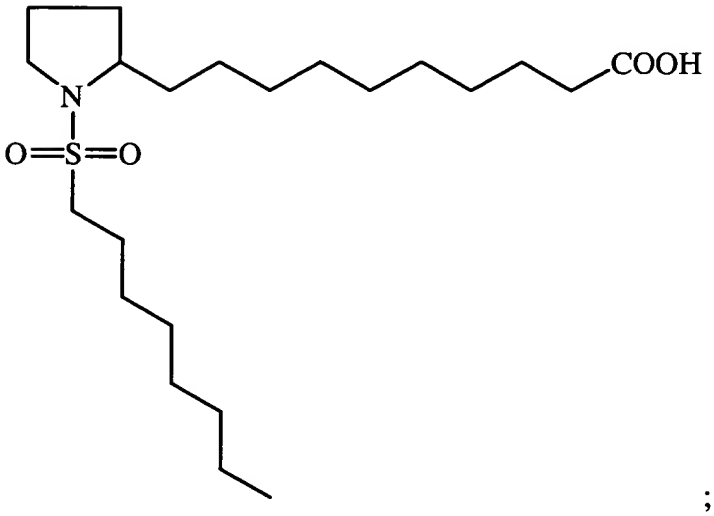
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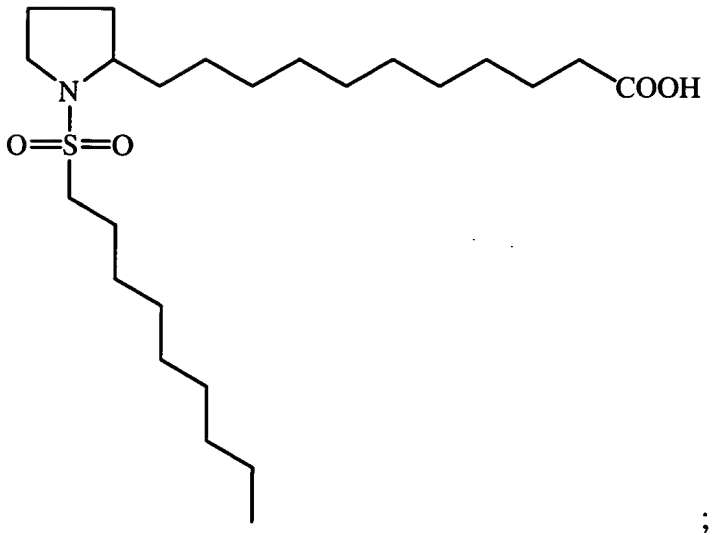
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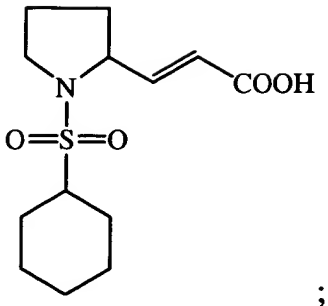
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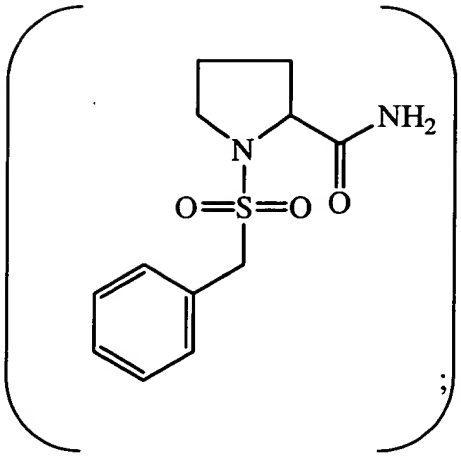

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